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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,250	02/17/2004	Yogendra Singh	4752-103.1 US	1479

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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,250	SINGH ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 8-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-25 are pending.

Claim 7 is under consideration; all other claims are herein withdrawn from consideration.

Information Disclosure Statement

1. The information disclosure statement filed July 15, 2004 has not considered.

Election/Restriction

2. Applicant's election without traverse of Group II, claim 7 in the reply filed on August 25, 2005 is acknowledged.

3. Claims 1-6 and 8-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups I, III-IV, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 25, 2005.

Claim Objections

4. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 7 depends from claim 1; claim 1 reciting SEQ ID NO 1. SEQ ID NO 1 is representative of an amino acid sequence of 735 amino acids. Claim 7 recites the following combination of claim limitations "The gene encoding the recombinant protein PA-I, defined in claim 1, having sequence SEQ ID NO 4. SEQ ID NO 4 is a 69 base polynucleotide sequence that encodes 23 amino acids. Claim 7 broadens the scope of claim 1 by redefining the invention

to be directed to a gene that only encodes 23 amino acids. Therefore claim 7 is broader in scope than the claim from which it depends; claim 7 recites a coding sequence for a fragment recombinant protein rather than the full-length recombinant protein of claim 1.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 7 is directed to "The gene encoding". The claimed gene is not isolated and purified and therefore reads on a product of nature. The claimed invention is directed to non-statutory subject matter. While claims 1 and 7 recite the term "recombinant", natural recombination takes place in nature.

7. Additionally, this rejection is being made of record in light of the fact that SEQ ID NO 4, is much smaller in size than the coding sequence for SEQ ID NO 1 and the scope of claim 7 encompasses coding sequences for fragments of the larger recombinant protein of claim 1. "The gene" of claim 7 need not encode the entire recombinant protein of claim 1, but need only be a gene "having sequence SEQ ID NO 4". Therefore, claim 7, as now claimed reads on a product of nature. This rejection could be obviated by amending the claim to recite ------isolated and purified------.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 7 is dependent from a withdrawn claim and therefore does not distinctly claim Applicant's invention.

b. Claim 7 also recites the phrase "having sequence SEQ ID NO 4"; this term lacks antecedent basis in claim 1 from which it depends. SEQ ID NO 1 recited in claim 1 is an amino acid sequence and SEQ ID NO 4 is a polynucleotide sequence. An amino acid sequence does not provide antecedent basis for a polynucleotide sequence.

c. Claim 7 recites the phrase "The gene" and depends from claim 1 which is directed to a protein. The phrase "The gene" lacks antecedent basis in claim 1.

1. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (scope). This is a *written description rejection.*

The instantly claimed invention is directed to a genus of "genes" encoding recombinant PA-I having the sequence of SEQ ID NO 4. Bacterial genes comprise not only the coding sequence for a protein, but are also in association with regulatory sequences in an operon.

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can

reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The claimed invention is directed to bacterial genes that comprise SEQ ID NO 4, which is a partial open reading frame that encodes for 23 amino acids from Clostridium perfringens iota Ib toxin, and the genes claimed must encode an anthrax inhibitory dominant negative mutant protein, PA-I protein.

PA-I having been defined in the instant Specification to encompass:

- "PCR based mutagenesis of PA gene resulting into dominant negative mutant of PA, purification of mutant PA protein from B. anthracis, cytotoxicity assay, in vitro inhibition of pore-forming ability of wild-type PA by PA-I for demonstrating defective channel formation (see page 4, paragraph 4).

Additionally, the claimed invention is defined in the instant Specification to be:

- "PA-I has 23 amino acids from iota-b toxin"

and by stating:

- "The main feature of the invention is replacement of bolded part of PA sequence with blue part of the iota b toxin sequence to get the PA-I."

Therefore the genus of genes now claimed must comprise SEQ ID NO 4, and may comprise any number codons that are produced by PCR based mutagenesis which results in a dominant negative mutant of PA which can be selected by in vitro inhibition of pore-forming ability and channel formation. What these mutant genes are have not been described.

With the exception of the isolated polynucleotide coding sequence for SEQ ID NO 1, which comprises the translated amino acid sequence of SEQ ID NO: 2, SEQ ID NO 2 encoded

by SEQ ID NO 4, the skilled artisan cannot envision the detailed structure of the recombinant protein with the recited functional characteristics.

While the instant Specification does disclose an isolated polynucleotide that encodes SEQ ID NO 1 which is mutant protective antigen of anthrax toxin that comprises 23 amino acids of iota Ib toxin inserted at positions 302-325, the amino acids encoded by SEQ ID NO 4, no other polynucleotide sequences that encode a dominant negative mutant anthrax protective antigen (PA) containing the coding sequence SEQ ID NO 4 of iota toxin Ib have been described.

The specification does not provide written descriptive support for the claimed invention directed to a genus of genes that encode a "novel molecule" that function as inhibitors, that include SEQ Id NO 4, which encodes the "amino acid sequence of SEQ ID NO 2" .

A description of a genus may be achieved by means of a recitation of a representative species, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. A recombinant nucleic acid molecule encodes a recombinant protein. Consistent with this fact, the court held in the decision *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412, 1406 (Fed. Cir. 1997), that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by

structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

There is no description, however, of what these mutations are that would result in a dominant negative mutant other than the single species described by SEQ ID NO 1. A representative number of species for the claimed genus of coding sequences/genes for PA-I protein molecules that comprise various mutations that result in the required functional characteristics and include SEQ ID NO 4, and result in the desired phenotype, have not been described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no description of where or how the alterations must be made in the gene loci to achieve the recited effect. The specification proposes to discover other members of the genus by using sequence homologies and introduction of alterations based upon what is already known, and processes the translated proteins in a screening assay.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more

than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

There is insufficient to support for generic claim 7 as provided by the Interim Written Description Guild lines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore only an isolated polynucleotide coding sequence for a recombinant protein of about 85.2 kDa, which comprises Anthrax protective antigen with a 2B2-2B3 loop of SEQ ID NO 2, SEQ Id NO 2 encoded by SEQ ID No 4, and functions as a dominant negative inhibitor of anthrax toxin in vivo, has been disclosed and described, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 U.S.C. § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Sirard et al (June 1997).

Sirard et al discloses the instantly claimed invention directed to a coding sequence that encodes the "amino acid residues of the amphipathic loop of the homologous toxin iota", the coding sequence encoding SEQ Id NO 2, encoded by a polynucleotide sequence that comprises

codons the same as or equivalent to SEQ ID NO 4. (see page 2029, col. 2, paragraph 2; page 2030, col. 1, paragraph 5).

The recombinant gene encoded a recombinant protein comprised a 2B2-2B3 loop, as the recombinant protein was the entire iota toxin Ib component and would inherently comprise the coding sequence SEQ ID NO 2 (96 kDa form, see page 2030, paragraph 5) which is encoded by codons which are the same or equivalent codons of SEQ ID NO 4.(see page 2032, col. 1, paragraphs 2-4; see title, abstract, page 2029, col. 1, paragraph 1 where PA antigen is defined to be encoded by "pag" gene, and page 2029, col. 2, paragraph 2, where the article defines "a gene fusion between the pag gene promoter and the *ibp* gene, encoding Ib"). The reference anticipates the instantly claimed invention in light of the combination of claim limitations set forth in claim 7 , that are unclear and read on the disclosure of Sirard et al.

3. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

4. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US006592872B1 US 20030198651A1 US 20020048590A1 are cited to show compositions comprising anthrax protective antigen or iota protective antigen together with an additional antigen.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
December 1, 2005

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